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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,383	02/05/2002	Marco Thyes	0480-01211	2952
26474	7590	05/26/2004	EXAMINER	
KEIL & WEINKAUF 1350 CONNECTICUT AVENUE, N.W. WASHINGTON, DC 20036			OH, TAYLOR V	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/889,383

**Applicant(s)**

THYES ET AL.

**Examiner**

Taylor Victor Oh

**Art Unit**

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 September 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/2001</u> . | 6) <input type="checkbox"/> Other: _____  |

The Status of Claims

Claim 1 is pending.

Claim 1 has been rejected.

**DETAILED ACTION**

1. Claim 1 is under consideration in this Office Action.

**Drawings**

2. None.

***Claim Rejections - 35 USC § 103***

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Warner Lambert Pharmaceutical Co.(GB 1226318).

**1. *Determining the scope and contents of the prior art***

Warner Lambert Pharmaceutical Co discloses a process for reducing the content of ethyl 3-dimethylamino-2-phenylpropionate in a mixture containing ethyl 2 –

Art Unit: 1625

dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate, which has been exemplified in the following (see col.4, lines 25 -70) :

#### EXAMPLE 1

##### (A) Separation Procedure

In this example, 40.2 grams (0.32 mol) of oxalic acid dihydrate, 281.0 grams of a mixture containing 3 - *cis* - dimethylamino - 4 - phenyl - 4 - *cis* - carbethoxy -  $\Delta^1$  - cyclohexene and 3 - *trans* - dimethylamino - 4 - phenyl - 4 - *trans* - carbethoxy -  $\Delta^1$  - cyclohexene and 460 ml of n-butyl alcohol were charged into a suitable reaction vessel. It had been determined by gas liquid chromatography that the isomeric mixture employed contained 28.1%, equivalent to 79.0 grams (0.29 mol) of the *trans*- isomer. The reaction mixture was heated to a temperature of about 85° C. and it was maintained at that temperature until a solution resulted. The heating time was about 15 minutes. The solution, thus obtained, was cooled to a temperature of about 5° C. and 3 - *trans* - dimethylamino - 4 - phenyl - 4 - *trans* - carbethoxy -  $\Delta^1$  - cyclohexene oxalate came out of solution in the form of a precipitate. In order to insure complete precipitation of the oxalate salt of the *trans*- isomer, the reaction mixture was maintained at a temperature within the range of from about 0° C. to about 5° C. for a period of about one hour. At the end of that period, the oxalic acid salt of the *trans*- isomer was collected by filtration. The salt was, thereafter, washed two times using 70 ml. of cold n-butyl alcohol each time. The salt was subsequently dried at a temperature of 65° C. and there was obtained 96.5 grams (0.266 mol) of 3 - *trans* - dimethylamino - 4 - phenyl - 4 - *trans* - carbethoxy -  $\Delta^1$  - cyclohexene oxalate having a melting point at 124.5° C. to 127° C. The yield of the oxalic acid salt of the *trans*- isomer obtained was equivalent to 72.5 grams of 3 - *trans* - dimethylamino - 4 - phenyl - 4 -

*trans* - carbethoxy -  $\Delta^1$  - cyclohexene in the form of the free base. Thin layer chromatography indicated the presence in the product of less than about 0.1% of the *cis*- isomer and less than about 0.25% of ethyl 2 - phenyl - 3 - dimethylaminopropionate.

Furthermore, in the separation procedure, a ratio of from 1 to 1.2 mol of oxalic acid or fumaric acid per each mol of *trans*-isomer present in the isomeric mixture (see col. 2, lines 99-102).

Moreover, the ethyl 2 –dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate compound has been known for having a therapeutic activity as analgesics (see first page, lines 60-66).

**2. *Ascertaining the differences between the prior art and the claims at issue***

The instant invention, however, differs from the prior art in that the claimed content of ethyl 3-dimethylamino-2-phenylpropionate in the mixture is less than 0.1 %.

**3. *Resolving the level of ordinary skill in the pertinent art***

Even so, the prior art does teach that the content of ethyl 3-dimethylamino-2-phenylpropionate present in the final product (a trans form of ethyl 2 –dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate) is less than 0.25 % in the mixture (see col. 4, lines 69-70). Therefore, it would have been obvious to the skilled artisan in the art to have motivated to reduce its content of impurity further to a less than 0.1 % in order for the desired final product to be used as a safe analgesic drug.

**4. *Considering objective evidence present in the application indicating obviousness or nonobviousness***

Warner Lambert Pharmaceutical Co does disclose the process for reducing the content of ethyl 3-dimethylamino-2-phenylpropionate to a less than 0.25 % in the mixture (see col. 4, lines 69-70) containing ethyl 2 –dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate; furthermore, it is well-known that the ethyl 2 –dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate compound has possessed the therapeutic activity as analgesics. Therefore, it would have been obvious to the skilled artisan in the art to have motivated to reduce its content of impurity further to a less than

Art Unit: 1625

0.1 % for purpose of using the desired final product as a safe analgesic drug. This is because the skilled artisan in the art would expect the purest compound to be the safest drug suitable for the therapeutics.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Mckane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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5/20/04

Ba K. Trinh

BA K. TRINH  
PRIMARY EXAMINER  
GROUP 1200 1625